Hashimoto's Encephalopathy: Back to Square One

Lord Brain and colleagues' classic description is cautiously entitled "Hashimoto's Disease and Encephalopathy." At the end of their discussion, the authors concluded that "antibody studies in future cases of unexplained encephalopathy should show whether we have described a syndrome or a coincidence."[1] At present, more than 250 additional adult cases with "Hashimoto's encephalopathy" (HE) have been reported in the literature, revealing a wide clinical spectrum, including movement disorders such as myoclonus (>20% of patients), ataxia, tremor, and opsoclonus.[2,3] It has been suggested that this condition be referred to as steroid-responsive encephalopathy and associated autoimmune thyroiditis (SREAT), given that the role of anti-thyroid autoantibodies (ATAs) is far from clear.[2] However, at the same time, this new name implies steroid responsiveness, which is not always the case.[2,4]

In an effort to solve the riddle that this condition entails, Mattozzi and colleagues recently conducted a study to determine whether pretreatment diagnostic criteria for HE predict steroid responsiveness.[4] They included 24 patients (14 women) with suspected HE and only six of them completely responded to steroids.[4] In addition, the authors reported that serum thyroid peroxidase (TPO) autoantibodies had a very limited specificity for this condition, because they were also detected in 8.1% and 8.2% of patients with possible autoimmune encephalitis and control subjects, respectively.[4] Finally, only one patient with suspected HE had autoantibodies against the amino-terminal of alpha-enolase (NAE),[4] a serum biomarker that had previously been reported to have high specificity for this condition.[3] NAE autoantibodies were also detected in one control subject.[4]

In view of these findings, it seems we are back at square one. Considering the lack of steroid responsiveness in the majority of cases, the term SREAT seems to be a misnomer. Given ATAs are not specific for the disease, "Hashimoto's disease *and* encephalopathy" (rather than HE) seems an appropriate description. Most likely, Hashimoto's disease *and* encephalopathy is not a single disease entity but a clinical spectrum of as yet unexplained encephalopathies with different underlying pathomechanisms. ATAs probably only reflect a general susceptibility to autoimmunity, as Becker and colleagues suggested more than 5 decades ago.[5]

For the present, it important to keep this in mind and search for disease-defining autoantibodies in any such patient. Particularly, although not exclusively, encephalitis with $GABA_AR$-autoantibodies frequently associates with thyroid autoimmunity. Further studies to define homogenous subgroups will be needed to find specific biomarkers and to understand the underlying pathophysiological mechanisms.

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